Interventions to Prevent Post-Traumatic Stress Disorder
A Systematic Review

Catherine A. Forneris, PhD, ABPP, Gerald Gartlehner, MD, MPH, Kimberly A. Brownley, PhD, Bradley N. Gaynes, MD, MPH, Jeffrey Sonis, MD, MPH, Emmanuel Coker-Schwimmer, MPH, Daniel E. Jonas, MD, MPH, Amy Greenblatt, BA, Tania M. Wilkins, MS, Carol L. Woodell, BSPH, Kathleen N. Lohr, PhD, MPhil, MA

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Context: Traumatic events are prevalent worldwide; trauma victims seek help in numerous clinical and emergency settings. Using effective interventions to prevent post-traumatic stress disorder (PTSD) is increasingly important. This review assessed the efficacy, comparative effectiveness, and harms of psychological, pharmacologic, and emerging interventions to prevent PTSD.

Evidence acquisition: The following sources were searched for research on interventions to be included in the review: MEDLINE; Cochrane Library; CINAHL; EMBASE; PILOTS (Published International Literature on Traumatic Stress); International Pharmaceutical Abstracts; PsycINFO; Web of Science; reference lists of published literature; and unpublished literature (January 1, 1980 to July 30, 2012). Two reviewers independently selected studies, extracted data or checked accuracy, assessed study risk of bias, and graded strength of evidence. All data synthesis occurred between January and September 2012.

Evidence synthesis: Nineteen studies covered various populations, traumas, and interventions. In meta-analyses of three trials (from the same team) for people with acute stress disorder, brief trauma-focused cognitive behavioral therapy was more effective than supportive counseling in reducing the severity of PTSD symptoms (moderate-strength); these two interventions had similar results for incidence of PTSD (low-strength); depression severity (low-strength); and anxiety severity (moderate-strength). PTSD symptom severity after injury decreased more with collaborative care than usual care (single study; low-strength). Debriefing did not reduce incidence or severity of PTSD or psychological symptoms in civilian traumas (low-strength). Evidence about relevant outcomes was unavailable for many interventions or was insufficient owing to methodologic shortcomings.

Conclusions: Evidence is very limited regarding best practices to treat trauma-exposed individuals. Brief cognitive behavioral therapy may reduce PTSD symptom severity in people with acute stress disorder; collaborative care may help decrease symptom severity post-injury.
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Context

Traumatic events affect millions of lives annually; societal awareness of the impact of trauma has increased over the past decade. Large-scale events include war, along with natural and manmade disasters; other events occur more regularly and on a much smaller scale, such as motor vehicle accidents, sexual assault, domestic violence, and gang shootings. An individual can experience trauma by witnessing another person experiencing trauma, by learning about trauma experienced by a family member or close associate, or directly.

From the Department of Psychiatry (Forneris, Brownley, Gaynes), the Department of Social Medicine and the Department of Family Medicine (Sonis), the Department of Medicine (Jonas), and the Cecil G. Sheps Center for Health Services Research (Gaynes, Coker-Schwimmer, Jonas, Wilkins), University of North Carolina, Chapel Hill; RTI International (Gartlehner, Greenblatt, Woodell, Lohr), Research Triangle Park, North Carolina; Department for Evidence-based Medicine and Clinical Epidemiology (Gartlehner), Danube University, Krems, Austria

Address correspondence to: Catherine A. Forneris, PhD, ABPP, University of North Carolina at Chapel Hill, Department of Psychiatry, CB# 7160, Chapel Hill NC 27599-7160. E-mail: Catherine_Forneris@med.unc.edu.

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Shortly after exposure, many people experience various symptoms of post-traumatic stress disorder (PTSD), such as flashbacks, emotional numbing, and difficulty sleeping. PTSD symptoms almost always emerge within days of the exposure (usually within 3 months of the event).[1] In most people, symptoms resolve within several weeks of exposure. However, PTSD develops in a substantial minority (up to one third) of those exposed to trauma.[2] Although approximately 50% of those diagnosed with PTSD improve without treatment within 1 year, 10%–20% develop a chronic unremitting course.[3–5] The relative pervasiveness of traumatic events and their adverse impact on individuals in both the short and long term means that clinicians regularly encounter trauma victims, even if that is not the reason the victims are seeking care. Clinicians are then faced with identifying, diagnosing, and treating patients with symptoms of PTSD and other associated psychiatric disorders.[6–9]

Post-traumatic stress disorder requires an identifiable precipitating event, so prevention is a compelling strategy to reduce incidence and mitigate symptoms.[10] "Universal" prevention strategies deliver interventions to all people who have recently been exposed to a trauma, regardless of symptoms or risk of developing PTSD. "Targeted" strategies identify people at high risk of developing PTSD after exposure to trauma and intervene among them only.

See related Commentary by Stein and Lang in this issue.

Research has identified characteristics of people, traumatic events, and social environments that increase the probability of PTSD, but no validated clinical prediction rule is available to identify people at high risk.[11] Thus, clinicians' ability to offer targeted interventions is limited. Moreover, lack of evidence-based clinical guidelines has led to ongoing, widespread use of some strategies, such as debriefing, despite data indicating that they do not prevent PTSD and might even cause harm.[12]

Prevention has a potential monetary benefit as well. One report estimated large treatment cost savings if 100% of military personnel needing care for PTSD and depression received evidence-based care.[13] For instance, the cost of depression, PTSD, or co-existing PTSD and depression could be reduced by as much as $1.7 billion ($1063 per returning veteran) by increasing productivity and decreasing expected number of suicides. If such savings can be realized from treating these disorders, then preventing PTSD could conceivably be even better in terms of both financial and biopsychosocial patient burden.

For the U.S. Agency for Healthcare Research and Quality (AHRQ), the RTI–University of North Carolina at Chapel Hill Evidence-based Practice Center (EPC) conducted a systematic review and meta-analysis of the efficacy, comparative effectiveness, and harms of psychological, pharmacologic, and emerging interventions to prevent PTSD in adults following trauma exposure.[14] The many approaches that clinicians might consider for use or referral include: psychological interventions, such as cognitive behavioral therapy (CBT, and many variants) or debriefing; pharmaceutic interventions, such as second-generation antidepressants, beta-blockers, and steroids; and emerging interventions, such as complementary and alternative medicine or collaborative care strategies (which involves close cooperation between non-mental-health and mental-health clinicians in organizing care management and judiciously using evidence-based pharmacologic and psychotherapy interventions). The current article summarizes the review's primary findings, highlights clinical implications, and offers recommendations for future research. Companion reports cover treatment of child and adult PTSD, respectively.[15,16]

Evidence Acquisition

Data Sources and Searches

In accordance with a formal protocol, the EPC team searched MEDLINE; the Cochrane Library; EMBASE; CINAHL; PILOTS (Published International Literature on Traumatic Stress); International Pharmaceutical Abstracts; PsycINFO; and Web of Science, from January 1, 1980 to July 30, 2012. The search was limited to English-language and human-only studies (Appendixes A–D, available online at www.ajpmonline.org). The EPC team used medical subject headings (as defined in these sources) as search terms when available, and key words when appropriate, focusing on terms to describe relevant populations and treatments. The team manually searched reference lists of pertinent reviews to identify possibly missing citations and sought unpublished studies through August 21, 2012, using ClinicalTrials.gov, the U.S. Food and Drug Administration website, the WHO International Clinical Trials Registry Platform, Grey Matters, and OpenGrey.[14]

Study Selection

The EPC team developed inclusion/exclusion criteria for variables relating to populations, interventions, comparators, outcomes, timing, settings, and study designs. Eligible studies had to: (1) enroll adults aged ≥18 years who had been exposed to trauma; (2) compare a preventive intervention (either targeted or universal) administered within 3 months of the traumatic exposure with waitlist, usual care, no intervention, placebo, or another psychological, pharmacologic, or emerging intervention (Appendix E, available online at www.ajpmonline.org); and (3) assess either incidence of PTSD (i.e., preventing PTSD) or severity of PTSD symptoms (Table 1).

To evaluate intervention benefits, the review included RCTs, nonrandomized controlled trials, and prospective controlled cohort studies; for harms (e.g., unexpected worsening of PTSD symptoms or reports of adverse events following intervention), the review also included retrospective controlled cohort studies and case–control studies. Two investigators independently reviewed

Table 1. Diagnostic and symptom severity measures for PTSD

Abbreviated name	Complete name	Range of possible scores	Improvement indicated by
CAPS	Clinician-Administered PTSD Scale	0–136	Decrease
CIDI-PTSD	PTSD module of the Composite International Diagnostic Interview	NA (dichotomous measure not meant to produce PTSD symptom severity score)	NA (measure does not produce a score)
IES	Impact of Event Scale	0–75	Decrease
IES-R	Impact of Event Scale–Revised	0–88	Decrease
MINI-PTSD	PTSD module of the Mini International Neuropsychiatric Interview	NA (dichotomous measure not meant to produce PTSD symptom severity score)	NA (measure does not produce a score)
PCL	PTSD Checklist	17–85	Decrease
PDS or PTDS	Post-Traumatic Diagnostic Scale	0–51	Decrease
PHSI-P	Post-Hospital Stress Index for Parents	0–20	Decrease
PSS	PTSD Symptom Scale	0–51	Decrease
PTSS-10	Post-Traumatic Stress Symptom 10 Question Inventory	10–70	Decrease
SI-PTSD	Structured Interview for PTSD	0–68	Decrease

NA, not applicable; PTSD, post-traumatic stress disorder

abstracts and full texts of relevant articles against predefined eligibility criteria. They resolved conflicts by consensus or with a third senior team member.

Data Extraction and Risk of Bias Assessment

A member of the EPC team recorded pertinent information on the variables noted above on structured forms. A second member reviewed all data extractions for completeness and accuracy. Two reviewers independently assessed study risk of bias (as low, medium, or high) against predefined, study design–specific criteria,[17] with disagreements resolved as above. The EPC team omitted studies with a high risk of bias from the main data synthesis (Appendix F, available online at www.ajpmonline.org) but used them in sensitivity analyses. In cases in which relevant information was unclear or was not reported, reviewers attempted to contact authors to get additional or unpublished information. When successful, the EPC team included such information in the analyses.

Data Analysis

The EPC team used random effects models (per DerSimonian and Laird)[18] for meta-analyses of outcomes reported by multiple studies whose interventions and populations were sufficiently similar to justify combining their results; analyses were conducted using Stata 11.1. The team's chosen effect measures were the weighted mean difference for continuous outcomes and relative risks for dichotomous outcomes. For all meta-analyses, the team conducted sensitivity analyses both with and without the inclusion of studies with a high risk of bias, using chi-square and I^2 statistics to assess statistical heterogeneity.[19,20] When quantitative analyses were inappropriate, the team synthesized data qualitatively.

To grade the strength of evidence, two reviewers (one a senior investigator) first independently assessed four domains—risk of bias, consistency, directness, and precision—for each major comparison and outcome. From this, an overall strength-of-evidence grade of high, moderate, low, or insufficient was assigned, corresponding to the confidence the team had in the likelihood that reported effect estimates reflected a true effect estimate and would be stable over time or with additional research.[21] Differences were resolved as above. All analytic steps took place between January and September 2012.

Evidence Synthesis

The review's searches identified 2563 citations; of these, the EPC team considered 56 studies and retained 19 studies that had low or medium risk of bias for the main data synthesis (Figure 1). All were RCTs (some with multiple arms; Table 2[22–39] and E Wong, PhD, The RAND Corporation, personal communication, 2012).

Efficacy of Psychological Interventions

Of the 16 studies investigating psychological interventions[22–36] (and E Wong, PhD, The RAND Corporation, personal communication, 2012), 11 assessed efficacy for preventing PTSD or reducing PTSD symptoms (Table 3). These interventions included Battlemind training, CBT, CBT plus hypnosis, cognitive therapy, debriefing, prolonged exposure therapy, psychoeducation, self-help materials, and supportive counseling.[22,23,28,29,31–36,38,39] (E Wong, PhD, The RAND Corporation, personal communication, 2012). For most interventions, the body of evidence consisted of single studies, often with small

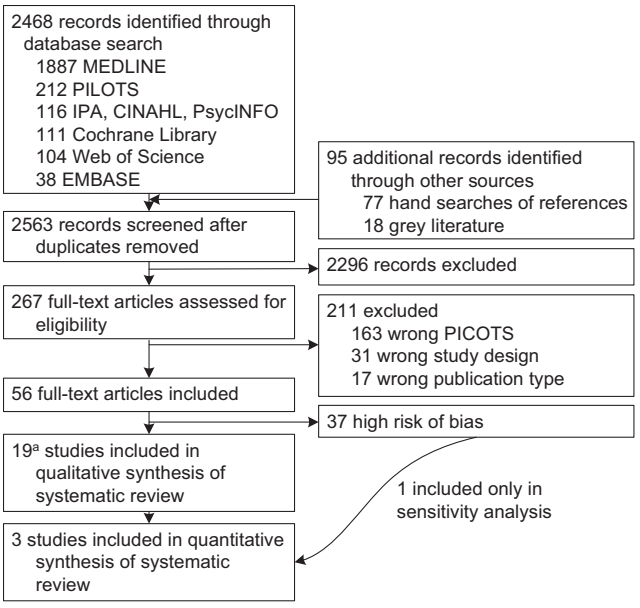

Figure 1. Summary of evidence search and selection of articles about prevention of post-traumatic stress disorder

[a]One article identified through gray literature searches is from E Wong, PhD, The RAND Corporation, personal communication, 2012. CINAHL, Cumulative Index to Nursing and Allied Health Literature; EMBASE, Excerpta Medica Database; IPA, International Pharmaceutical Abstracts; PICOTS, patient populations, interventions, comparators, outcomes, timing, and settings; PILOTS, Published International Literature on Traumatic Stress

sample sizes, methodologic limitations, and imprecise results, thus precluding the EPC team from drawing efficacy conclusions.

Debriefing was the only type of intervention with sufficient evidence on which to base conclusions with some degree of confidence. Two debriefing studies in civilian trauma samples[32,36] used debriefing based on Mitchell's Critical Incident Stress Debriefing protocol,[40] originally developed for individuals indirectly exposed to traumatic events because of occupation (e.g., firefighters or emergency medical personnel).[40,41,42]

Debriefing (versus controls) did not reduce either PTSD incidence or PTSD symptom severity at multiple follow-up intervals spanning 2 weeks to 11 months (low strength of evidence for no differences in benefit).[32,36] At 6 months, PTSD incidence (Post-Traumatic Stress Scale) was 23% vs 26% (p not reported); PTSD symptom severity (Impact of Event Scale) was 19.7 vs 23.3 (p not reported).[32] Also at 6 months, PTSD symptom severity (Structured Interview for PTSD) was 10.2, 9.3, and 9.6 in those receiving emotional debriefing, educational debriefing, and no debriefing, respectively ($p=0.33$).[36] Debriefing did not decrease symptoms of depression or anxiety.[36]

Efficacy of Pharmacologic Interventions

Two trials assessed the efficacy of a specific pharmaceutic agent: escitalopram[35] (a selective serotonin reuptake inhibitor) and hydrocortisone[38] (Table 3). Because of small sample size, evidence was insufficient to permit any conclusions about primary outcomes. In a third trial, dosing of sedation (light vs deep) in critically ill patients did not affect post-traumatic symptoms, depression, or anxiety (insufficient evidence).[37]

Efficacy of Collaborative Care

One single-blind trial addressed collaborative care in 207 victims of trauma who required surgical hospitalization and screened positive for PTSD symptoms on two separate occasions within 1 month of the trauma (Table 3).[39] Eligible patients received 12 months of either a stepped, collaborative care intervention (care management, evidence-based pharmacologic interventions, CBT components) or usual care (control). The collaborative care group exhibited significantly lower PTSD symptom severity on the Clinician-Administered PTSD Scale at 6 and 12 months after injury and on the PTSD Checklist–Civilian version at 6, 9, and 12 months after injury (low strength of evidence; Table 3). The groups did not, however, differ on reduction of PTSD symptom severity at 1 month or 3 months after injury, or on prevention of PTSD at 12 months.

Comparative Effectiveness of Psychological and Pharmacologic Interventions

Eight studies compared effectiveness of a psychological intervention with either a pharmacologic (Escitalopram[35]) or another psychological intervention (Table 2).[23–26 30,32,35,36] Most trials involved a single intervention with small sample sizes and no prior established efficacy. Evidence was insufficient to determine the comparative effectiveness of Battlemind training, cognitive therapy, debriefing, prolonged exposure therapy, and psychoeducation in preventing PTSD or reducing PTSD symptom severity (Table 3).

Three studies from the same Australian team[24–26] directly compared brief CBT (5–6 weeks) with supportive counseling in 105 civilian survivors of mixed trauma who had acute stress disorder (Table 3). Acute stress disorder symptoms overlap those of PTSD and occur within the first month after trauma, but acute stress disorder is more likely than PTSD to involve subjective feelings of unreality with respect to the outside world or one's sense of self and dissociative amnesia.[4] The CBT intervention included education about trauma reactions, progressive muscle relaxation training, imaginal exposure to traumatic memories, cognitive restructuring of fear-related beliefs, and graded in vivo exposure to avoided situations. The EPC team conducted meta-analyses

Table 2. Characteristics of studies of interventions to prevent PTSD and reduce PTSD symptom severity

Study, risk of bias, prevention type	Study design, intervention (*n*)	Treatment duration (follow-up duration)	Population and trauma type	Primary outcome measure and baseline score	Mean age and age range (years), % female
Beatty (2010)[22,a] Medium Universal	Unblinded RCT Self-help booklet (25) Information booklet (24)	Not reported (6 months)	Civilian female medical (newly diagnosed with breast cancer within previous month)	PSS-SR overall: 10.76[b]	55.2 (range not reported) 100
Bryant (1998)[24,c] Medium Targeted	Unblinded RCT Cognitive behavioral therapy (12) Supportive counseling (12)	Five 90- minute weekly individual sessions (6 months)	Civilian (motor vehicle or industrial accidents)	CIDI-PTSD: not reported	32.6[d] (range not reported) 58.3
Bryant (2003)[25,c] Medium Targeted	Unblinded RCT Cognitive behavioral therapy (12) Supportive counseling (12)	Five 90-minute weekly individual sessions (6 months)	Civilian (motor vehicle accidents or nonsexual assault)	CAPS-2: not reported	31.21[d] (range not reported) 66.7
Bryant (2005)[26,c] Medium Targeted	Unblinded RCT Cognitive behavioral therapy (33) Cognitive behavioral therapy combined with hypnosis (30)	Six 50-minute sessions (6 months)	Civilian (motor vehicle accidents or nonsexual assault)	CAPS-2: not reported	33 (range not reported) 60.9
Bryant (2008)[23a,c] Low Targeted	Outcome assessor–blinded RCT Prolonged exposure therapy (30) Cognitive therapy (30) Waitlist (30)	Five 90-minute sessions (6 months)	Civilian mixed (motor vehicle accident, “other trauma,” physical assault, and “other accident”)	CAPS-2: prolonged exposure therapy: 70.6; cognitive therapy: 66.8; waitlist: 63.6	Not reported 57.8[d]
Campfield (2001)[27,e] Medium Universal	Unblinded RCT Immediate debriefing (<10 hours; 36) Delayed debriefing (>48 hours; 41)	One 1- to 2-hour individual or group session (2 weeks post-robbery)	Civilian crime victims (robbery)	PDS: not reported	22.82[d] (18–32) 54.5
Gamble (2005)[28,a] Medium Universal	Outcome assessor– blinded RCT Supportive counseling (50) Control (53)	One 40- to 60-minute session within 72 hours of birth (3 months postpartum)	Civilian women (distressing or traumatic childbirth)	MINI-PTSD: not reported	28 (18–46) 100
Melnyk (2004)[29,a] Medium Universal	Unblinded RCT Creating Opportunities for Parent Empowerment (90) Control (84)	Not reported (12 months after discharge)	Civilian medical (mothers of critically ill children)	PHSI-P: not reported	31.2 (18–52) 100

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Table 2. Characteristics of studies of interventions to prevent PTSD and reduce PTSD symptom severity *(continued)*

Study, risk of bias, prevention type	Study design, intervention (*n*)	Treatment duration (follow-up duration)	Population and trauma type	Primary outcome measure and baseline score	Mean age and age range (years), % female
Mulligan (2012)[30,c] Medium Universal	Recruitment assessor–blinded RCT Battlemind training (1108) Standard briefing (1335)	One 45-minute group session (4-6 months)	United Kingdom military service members, mixed (combat-related traumatic events)	PCL-C median total score: Battlemind: 21; Standard briefing: 20	Not reported 1.7[d]
O'Donnell (2012)[31,a] Medium Targeted	Unblinded RCT Cognitive behavioral therapy (24) Usual care (22)	Four to ten 90-minute sessions (12 months)	Civilian mixed (transportation accidents, falls, assaults, work-related accidents, other forms of traumatic injury)	CAPS total score: cognitive behavioral therapy: 56.61; usual care: 60.73	35.9[d] (range not reported) 39.1[d]
Rose (1999)[32,a,c] Medium Universal	Unblinded RCT Debriefing + psycho-education (54) Psycho-education (52) Assessment only (51)	One 1-hour individual session (6 months)[f]	Civilian crime victims (actual or threatened physical or sexual assault, bag snatch)	PSS-SR: debriefing + psycho-education: 16.8; Psycho-education: 16.0; assessment: 15.6	35 (18–76) 24.8
Rothbaum (2012)[33,a] Medium Universal	Outcome assessor–blinded RCT Prolonged exposure therapy (69) Assessment only (68)	Three 60- minute individual sessions (4 weeks)[g]	Civilian mixed (sexual assault, nonsexual assault, motor vehicle accident, other unspecified)	PSS-I: not reported	31.5[d] (range not reported) 65
Ryding (2004)[34,a] Medium Universal	Unblinded RCT Supportive counseling (89) Control (73)	Two 2-hour group sessions (6 months)	Civilian medical (emergency Caesarean section)	IES: not reported	332 (19–44) 100
Shalev (2011)[35,a,c] Medium Targeted	Outcome assessor– blinded RCT Cognitive therapy (40) Prolonged exposure therapy (63) Escitalopram[h] (23) Placebo (23) Waitlist (93)	Prolonged exposure therapy and cognitive therapy: 12 weekly 90-minute individual sessions; Escitalopram and placebo: 10 mg twice daily (9 months)	Civilian mixed (terrorist attacks, motor vehicle accidents, work or other accidents)	CAPS total score: cognitive therapy: 71.78; prolonged exposure therapy: 73.59; Escitalopram: 79.83; placebo: 74.91; waitlist: 71.66	Not reported 52.1
Sijbrandij (2006)[36,a,c] Low Universal	Unblinded RCT Emotional debriefing (76) Educational debriefing (79) No debriefing (81)	Ten 45- to 60-minute individual sessions (6 months)	Civilian (assault or accident)	SI-PTSD: emotional debriefing: 19.9; educational debriefing: 19.9; no debriefing: 17.7	40.4[d] (range not reported) 48.7[d]

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Table 2. *(continued)*

Study, risk of bias, prevention type	Study design, intervention (*n*)	Treatment duration (follow-up duration)	Population and trauma type	Primary outcome measure and baseline score	Mean age and age range (years), % female
Treggiari (2009)[37,e] Medium Universal	Single-blinded RCT Light sedation (69) Deep sedation (68)	Not applicable (4 weeks post-discharge)	Civilian medical (mechanical ventilation)	IES-R and PCL: not reported	61.4[d] (range not reported) 23.5[d]
Weis (2006)[38,a] Medium Targeted	Double-blind RCT Hydrocortisone stress dose[i] (14) Placebo (14)	Dose given over 4 days (6 months)	Civilian medical (cardiac surgery)	PTSS-10: not reported	68.5[d] (63–73) 32.1[d]
Wong, the RAND Corporation, unpublished observations, (2012)[a] Medium Universal	Unblinded RCT Psycho-education (42) Control (37)	One 18-minute video (1 month)	Civilian mixed trauma (e.g., gunshot, falls, other unspecified) with physical injury	PCL: not reported	31.2[d] (range not reported) 16
Zatzick (2013)[39,a] Low Targeted	Single-blind RCT Collaborative care (104) Usual care (103)	12 months (12 months)	Civilian medical (trauma requiring surgical admission)	CAPS: not reported PCL-C: collaborative care: 50.5; usual care: 50.8	38.5 (range not reported) 47.8

[a]Evaluated efficacy
[b]Reported for the entire sample, not by treatment arm
[c]Evaluated comparative effectiveness
[d]Data not provided by the study authors; authors of the current paper did the calculations reported in the table.
[e]Evaluated impact of timing, intensity, or dosing, but not efficacy or comparative effectiveness
[f]Because of very high overall attrition (i.e., >40% at 11-month follow-up) in this study of debriefing and psychoeducation, all outcomes collected at that time point were rated as having a high risk of bias and are therefore not reported here.[32]
[g]Because of high overall attrition (i.e., >30% at 12-week follow-up) in this study of exposure-based therapy, all outcomes collected at that time point were rated as having a high risk of bias and are therefore not reported here.[33]
[h]Subjects in the pharmacologic arm were blinded as to whether they were receiving escitalopram or placebo.
[i]Loading dose of 100 mg over 10 minutes, followed by a continuous infusion of 10 mg/hour for 24 hours (post-operative day [POD]1); reduced to 5 mg/hour on POD 2, tapered to 3 doses of 20 mg on POD 3, and then 3 doses of 10 mg on POD 4

CAPS, Clinician Administered PTSD Scale; CAPS-2, Clinician Administered PTSD Scale-2; CIDI-PTSD, Composite International Diagnostic Interview, PTSD Module; IES, Impact of Event Scale; IES-R, Impact of Event Scale-Revised; MINI-PTSD, Mini-International Neuropsychiatric Interview-Post-Traumatic Stress Disorder; PCL, PTSD Checklist; PCL-C, PTSD Checklist–Civilian Version; PDS, Post-Traumatic Stress Diagnostic Scale; PHSI-P, Post-Hospital Stress Index for Parents; POD, postoperative day; PSS-SR, Post-Traumatic Stress Disorder Scale–Self-Report; PTSD, post-traumatic stress disorder; PTSS-10, Post-Traumatic Stress Symptom 10-Question Inventory; SI-PTSD, Structured Interview for PTSD

Table 3. Interventions to prevent PTSD and reduce PTSD symptom severity: results and strength of evidence

Efficacy	Intervention; population	Outcome	Results	Strength of Evidence
	Cognitive behavioral therapy; civilian, mixed trauma types[31]	Incidence of PTSD	Inconclusive, single trial (N=46)	Insufficient
		PTSD symptom severity	Inconclusive, single trial (N=46)	Insufficient
	Cognitive therapy; civilian, mixed trauma types[23,35]	Incidence of PTSD	Inconclusive, single trial (*n*=133)	Insufficient
		PTSD symptom severity	Inconclusive, two trials (*n*=193), inconsistent findings at different assessment intervals	Insufficient
	Collaborative care; civilian, mixed trauma types requiring hospitalization and screening positive for PTSD symptoms[39]	Incidence of PTSD	Inconclusive, single trial (N=207)	Insufficient
		PTSD symptom severity	Collaborative care produces a greater decrease in PTSD symptom severity at 6 months (CAPS, 42.9 vs 56.7**; PCL-C, 40.6 vs 49.9**); at 9 months (PCL-C, 40.2 vs 45.5**); and 12 months (CAPS, 38.6 vs 47.2*; PCL-C, 37.4 vs 42.5*) after injury compared with usual care (N=207)	Low
	Debriefing; civilian, mixed trauma types[32,36]	Incidence of PTSD	Debriefing not significantly different than control at multiple follow-up assessment intervals across two trials (*n*=341)	Low
		PTSD symptom severity	Debriefing not significantly different than control at multiple follow-up assessment intervals across two trials (*n*=341)	Low
	Escitalopram; civilian, mixed trauma types[35]	Incidence of PTSD	Inconclusive, single trial (*n*=139)	Insufficient
		PTSD symptom severity	Inconclusive, single trial (*n*=139)	Insufficient
	Exposure-based therapies; civilian, mixed trauma types[23,33,35]	Incidence of PTSD	Inconclusive, 3 trials (*n*=355), inconsistent findings at different assessment intervals	Insufficient
		PTSD symptom severity	Inconclusive, 3 trials (*n*=355) with different assessment intervals that prevent direct comparisons	Insufficient
	Hydrocortisone stress dose; civilians undergoing high-risk cardiac surgery[38]	Incidence of PTSD	Inconclusive, single trial (*n*=28)	Insufficient
		PTSD symptom severity	Inconclusive, single trial (*n*=28)	Insufficient
	Psychoeducation; civilian, victims of crime[32] and injury (E Wong, the RAND Corporation, unpublished observations, 2012)	Incidence of PTSD	Inconclusive, two trials (N=182) with different assessment intervals that prevent direct comparisons	Insufficient
		PTSD symptom severity	Inconclusive, single trial (*n*=103)	Insufficient
	Self-help materials; civilian, women newly diagnosed with breast cancer[22,a]	PTSD symptom severity	Inconclusive, single trial (N=49)	Insufficient

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Table 3. *(continued)*

Efficacy	Intervention; population	Outcome	Results	Strength of Evidence
	Supportive counseling; civilian, women experiencing mixed trauma types[28,29,34]	Incidence of PTSD	Inconclusive, single trial (N=103)	Insufficient
		PTSD symptom severity	Inconclusive, two trials (*n*=336), inconsistent findings at different assessment intervals using different outcome measures	Insufficient
Comparative effectiveness	Battlemind training vs standard briefing; United Kingdom military service members[30]	PTSD symptom severity	Inconclusive, single trial (*n*=2443)	Insufficient
	Cognitive behavioral therapy vs cognitive behavioral therapy combined with hypnosis; civilian, mixed trauma types[26]	Incidence of PTSD	Inconclusive, single trial (*n*=63)	Insufficient
		PTSD symptom severity	Inconclusive, single trial (*n*=63)	Insufficient
	Cognitive behavioral therapy vs supportive counseling; civilian, mixed trauma types with acute stress disorder[24–26]	Incidence of PTSD	Cognitive behavioral therapy not significantly different than supportive counseling at end of treatment (RR, 0.27, 95% CI=0.05, 1.29; I^2=72%) or at 6 months (RR, 0.46, 95% CI=0.21, 1.01; I^2=45%); three trials (*n*=105)	Low
		PTSD symptom severity	Greater reduction for cognitive behavioral therapy than for supportive counseling on IES-I at end of treatment (WMD,−7.85, 95% CI=−11.18,−4.53; I^2=1%) and at 6 months (WMD,−8.19, 95% CI=−11.79,−4.58; I^2=7%); three trials (*n*=105)	Moderate
			Greater reduction for cognitive behavioral therapy than for supportive counseling on IES-A at end of treatment (WMD,−14.04, 95% CI=−19.37,−8.71; I^2=53.8%) and at 6 months (WMD,−9.94, 95% CI=−15.06,−4.83; I^2=44.0%); three trials (*n*=105)	
	Cognitive behavioral therapy combined with hypnosis vs supportive counseling; civilian, mixed trauma types[26]	Incidence of PTSD	Inconclusive, single trial (*n*=54)	Insufficient
		PTSD symptom severity	Inconclusive, single trial (*n*=54)	Insufficient
	Cognitive therapy vs prolonged exposure therapy; civilian, mixed trauma types[23,35]	Incidence of PTSD	Inconclusive, two trials (*n*=163), inconsistent findings at different assessment intervals; one trial used a completer analysis	Insufficient
		PTSD symptom severity	Inconclusive, two trials (*n*=163), inconsistent findings at different assessment intervals; one trial used a completer analysis	Insufficient
	Cognitive therapy vs escitalopram; civilian, mixed trauma types[35]	Incidence of PTSD	Inconclusive, single trial (*n*=54)	Insufficient
		PTSD symptom severity	Inconclusive, single trial (*n*=54)	Insufficient

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Table 3. Interventions to prevent PTSD and reduce PTSD symptom severity: results and strength of evidence *(continued)*

Efficacy	Intervention; population	Outcome	Results	Strength of Evidence
	Emotional debriefing vs educational debriefing; civilian, mixed trauma types[36]	Incidence of PTSD PTSD symptom severity	Inconclusive, single trial (n=155) Inconclusive, single trial (n=155)	Insufficient Insufficient
	Prolonged exposure therapy vs escitalopram; civilian, mixed trauma types[35]	Incidence of PTSD PTSD symptom severity	Inconclusive, single trial (n=77) Inconclusive, single trial (n=71)	Insufficient Insufficient
	Psychoeducation vs debriefing combined with psychoeducation; civilian, crime victims[32]	Incidence of PTSD PTSD symptom severity	Inconclusive, single trial (n=106) Inconclusive, single trial (n=106)	Insufficient Insufficient
Impact of timing, intensity, and dosing	**Intervention; population**	**Impact of timing: outcomes**	**Impact of intensity or dosing: outcomes**	**Strength of evidence**
	Early vs delayed debriefing; civilian, robbery victims[27]	Fewer post-traumatic symptoms with early vs delayed debriefing (5.3 vs 14.3***), single study (N=77) Lower symptom severity on PDS with early vs delayed debriefing (6.9 vs 33.1***), single study (N=77)	Not applicable	Insufficient
	Light vs deep pharmacologic sedation; civilian, critically ill patients[37]	No evidence	Dosing: 1 RCT (N=137) Similar rates of PTSD, depression, and anxiety symptoms with light and deep sedation	Insufficient
Subgroup analyses	**Subgroup; intervention, population**	**Outcome**	**Results**	**Strength of Evidence**
	Demographic groups: gender; cognitive behavioral therapy, debriefing; civilian, crime victims[27,32]	PTSD symptom severity	Consistent findings, two trials (N=234); gender did not modify the effect of cognitive behavioral therapy or debriefing	Low

(continued on next page)

Table 3. *(continued)*

Efficacy	Intervention; population	Outcome	Results	Strength of Evidence
	Type of trauma; prolonged exposure therapy; civilian, mixed trauma types[33]	Incidence of PTSD PTSD symptom severity	Inconclusive, single study (N=137) Inconclusive, single study (N=137)	Insufficient Insufficient
	Psychiatric diagnosis: previous depression; debriefing; civilian, crime victims[32]	PTSD symptom severity	Inconclusive, single study (N=157)	Insufficient
	History of child abuse[b]; psychoeducation vs debriefing combined with psychoeducation; civilian, crime victims[32]	PTSD symptom severity	Inconclusive, single study (N=157)	Insufficient
	Severity of baseline distress[b]; debriefing, self-help workbook; civilian: crime victims; women with breast cancer[22,36]	PTSD symptom severity	Inconsistent findings, two trials (N=285); one trial reported that debriefing increased PTSD symptoms among those with high baseline PTSD arousal symptoms, and one trial reported that a self-help workbook decreased PTSD symptoms to a greater extent in those with high baseline PTSD symptom severity.	Insufficient
	Severity of combat exposure[b]; United Kingdom military service members[30]	PTSD symptom severity	Inconclusive, single study (n=2443)	Insufficient
Risk of harms	Emotional debriefing vs no debriefing; civilian, medical trauma[36]	PTSD symptom severity	For subgroup with hyperarousal, inconclusive, single trial (N=236), inconsistent findings at different assessment intervals	Insufficient
	Light vs deep pharmacologic sedation[c]; critically ill patients[37]	Mortality Incidence of adverse events	Inconclusive, single trial (N=137) Inconclusive, single trial (N=137)	Insufficient Insufficient

[a]Incidence of PTSD not reported
[b]Personal risk factor for PTSD
[c]Open label study
*$p<0.05$, **$p<0.01$, ***$p<0.001$
CAPS, Clinician-Administered PTSD Scale; IES, Impact of Event Scale; IES-A, Impact of Event–Avoidance subscale; IES-I, Impact of Event Scale–Intrusions subscale; PCL-C, PTSD Checklist–Civilian Version; PDS, Post-traumatic Stress Diagnostic Scale; PTSD, post-traumatic stress disorder; RR, relative risk; SSRI, selective serotonin-reuptake inhibitor; WMD, weighted mean difference

for the incidence of PTSD and the severity of symptoms of PTSD, anxiety, and depression at the end of treatment and at 6-month follow-up (Appendix G, available online at www.ajpmonline.org).

Pooled results for PTSD incidence at 6-month follow-up favored CBT but did not reach significance (relative risk [RR] 0.46; 95 CI%=0.21, 1.01; Figure 2; low strength of evidence). Including a fourth study with high risk of bias in the meta-analyses produced a statistically significant relative risk reduction of >50% for the CBT patients (RR, 0.45; 95% CI=0.25, 0.82). Also at 6 months, scores on two Impact of Event subscales indicated that patients receiving CBT had a greater reduction in PTSD symptom severity than those receiving supportive counseling (both moderate strength of evidence): avoidance (−9.94; 95% CI= −15.06, −4.83; Figure 3) and intrusion (−8.19; 95% CI= −11.79, −4.58; Figure 4). Finally, those receiving CBT experienced numerically greater (but statistically nonsignificant) reductions in symptoms of anxiety and depression at 6 months (moderate and low strength of evidence for no difference with supportive care, respectively).

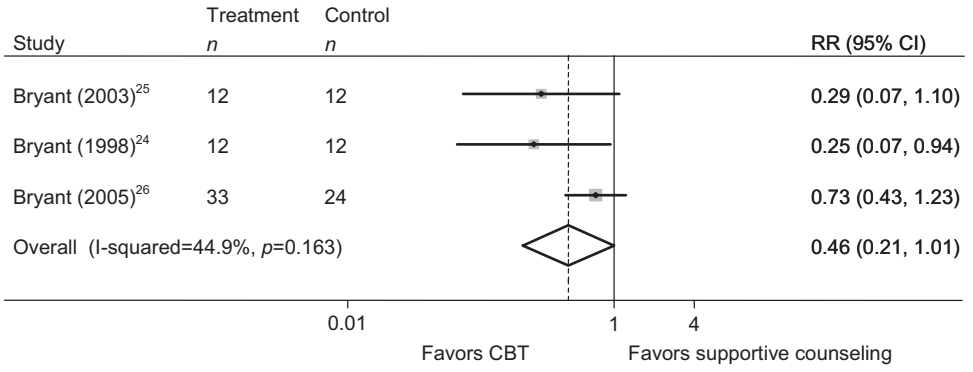

Figure 2. Mean change from baseline to 6-month follow-up in post-traumatic stress disorder incidence for cognitive behavioral therapy or supportive counseling
CBT, cognitive behavioral therapy; RR, relative risk

Subgroups

In two studies, debriefing had similar effects for men and women on PTSD symptom severity[27,32]; neither trial reported the magnitude of the estimated effect or its precision (low evidence of no difference by gender; Table 3). Two other studies provided inconsistent findings on whether baseline severity of PTSD symptoms modified the effect of two different psychological interventions for reducing PTSD symptom severity (insufficient strength of evidence).[22,36] Only single-study bodies of evidence evaluated outcomes in groups that differed in history of child abuse, previous depression, severity of combat trauma, and type of trauma; no differences were found in these studies (all insufficient evidence).[30,32,33]

Risk of Harms

Evidence was insufficient to draw conclusions about the risk of increased PTSD symptom severity following emotional debriefing or the risk of harms for any other psychological interventions (Table 3).[36] No trial of pharmacologic interventions provided information on intervention-associated risks. One open-label drug trial considered the comparative risk of mortality and incidence of adverse events, but results were inconclusive.[37]

Discussion

Preventing PTSD among adults exposed to various traumatic events is increasingly relevant for a wide range of healthcare providers, not just those in mental health settings. The number of individuals exposed to traumatic events is rising, and non-mental-health providers, such as emergency medicine physicians, face an increasing role in screening individuals for psychiatric symptoms. Evidence for best practices for treating trauma-exposed individuals is very limited, but results reported here (of

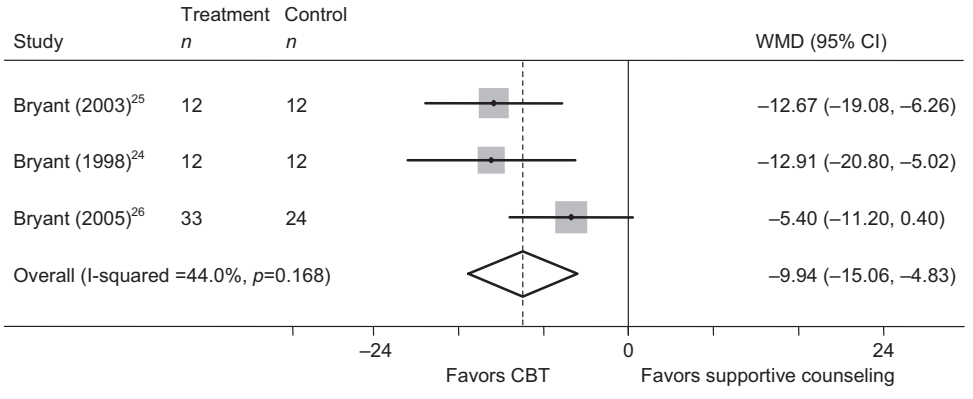

Figure 3. Mean change from baseline to 6-month follow-up in scores on the Impact of Event Scale–Avoidance Subscale, for CBT or supportive counseling
CBT, cognitive behavioral therapy; WMD, weighted mean difference

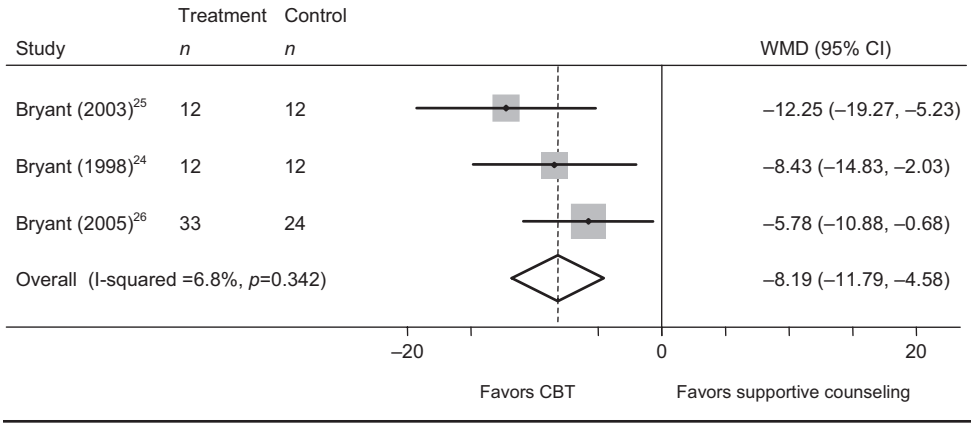

Figure 4. Mean change from baseline to 6-month follow-up in scores on the Impact of Event Scale–Intrusion Subscale, for CBT or supportive counseling
CBT, cognitive behavioral therapy; WMD, weighted mean difference

either low or moderate strength) suggest three tentative conclusions: (1) for people with acute stress disorder, CBT is more effective than supportive counseling in reducing PTSD symptom severity; (2) collaborative care produces a greater decrease in PTSD symptom severity after injury than usual care; and (3) generally, debriefing is not effective in reducing either PTSD incidence or the severity of PTSD or depressive symptoms. Only a subset of studies conducted clinical evaluations to determine PTSD diagnosis, leaving open the question of whether reducing symptom severity protects victims from developing PTSD. For all other interventions and outcomes of interest, evidence was either entirely lacking or insufficient to draw conclusions.

Applicability of Findings

Health professionals should view these findings cautiously, given the limited number of studies that met criteria for this review and the numerous deficiencies in reviewed studies. Although studies covered diverse populations with respect to trauma type and subjects' age, few or no studies dealt with victims of terrorism, sexual assault, natural disaster, or combat. Trials of pharmacologic interventions were scant. Studies varied widely in the time between trauma exposure and trial entry and used disparate eligibility criteria for PTSD symptomatology at study entry. Data were insufficient to draw conclusions about whether the response to intervention differs in people with versus without co-existing depression. These factors severely limit the applicability of these findings to specific subgroups such as racial or ethnic minorities, refugees, first responders, and individuals with co-existing psychiatric conditions or past history of other traumatic events.

Variability in the types of trauma and the contexts in which they occur, as well as differences among individuals exposed to traumatic events, will likely prohibit a "one size fits all" model for preventive intervention. Individuals respond differently to stress, and identifying persons at risk for PTSD, predicting who will develop PTSD, and successfully conducting early interventions in the aftermath of a traumatic event remain enormous challenges for the future.

Limitations

Three major limitations characterize evidence about psychological and pharmacologic interventions. First, published studies on the efficacy, comparative effectiveness, and harms of many interventions of interest simply were not found. Without efficacy evidence, assessing comparative effectiveness becomes impossible in most cases. Second, the existing literature has many methodologic shortcomings. Of the 56 studies potentially meeting eligibility criteria, 37 exhibited high risk of bias (i.e., low internal validity) for various reasons; this precluded considering them for the main analyses.[43] Third, selective availability of studies with positive results can seriously bias conclusions. Exploring publication bias for this review was quite restricted, despite extensive efforts to find all relevant studies or unpublished data.

Implications for Clinical Practice and Policy-Making

Increasingly, general medicine and primary care clinics function as the de facto mental healthcare system, serving as the main or only point of contact for individuals exposed to trauma.[6–9] Non-mental-health providers, including those with expertise in population management and public health, are increasingly playing a role in identifying individuals with psychiatric symptoms and disorders. Thus, they have the opportunity to intervene in the critical post-trauma window to prevent these patients from developing full-blown PTSD.

Unlike most psychiatric disorders, the precipitating cause of PTSD, psychological trauma, is an identifiable event with a known time and place of onset. Therefore, people at risk of developing PTSD can be identified, and preventive interventions can be offered to them shortly after exposure. Fulfilling this role presumes that clinicians and

public health professionals understand and have access to evidence-based treatments that they can initiate themselves or incorporate into mental health service delivery systems, such as pharmacologic and collaborative care interventions, or that they can appropriately refer patients for more specialized care.

Among people exposed to trauma who meet criteria for acute stress disorder, referring patients for CBT-based psychological treatment is warranted. However, that finding does *not* translate into a recommendation that healthcare providers screen all those exposed to trauma for this disorder, because it is a poor predictor of PTSD, and no studies demonstrate that people so screened have better outcomes than those not screened.[44] What clinicians can do is refer patients with worrisome symptoms for further assessment, ideally to a program that takes a comprehensive, collaborative care approach, including case management, pharmacotherapy, and CBT. Conversely, the current findings, consistent with those of other reviews, indicate that healthcare providers should not engage in debriefing interventions or refer patients to these types of interventions.

Preventing PTSD can potentially reduce substantial burdens, societal costs, and individual suffering. For example, the economic cost of the PTSD and depression cases among Operation Enduring Freedom/Operation Iraqi Freedom veterans alone (including medical care, forgone productivity, and lives lost through suicide) is estimated at $4–$6 billion over 2 years.[13] In addition to lives lost because of the increased risk of suicide, PTSD is associated with high medical costs and high social costs. PTSD is a strong risk factor for higher rates of psychiatric comorbidity; decreased functioning, such as poor work performance and associated job losses (on average, 3.6 days of work impairment per month); crime; and many other adverse consequences, such as reduced educational attainment, work earnings, and effects on marital stability, familial discord, and child rearing.[45]

Moreover, many people with PTSD do not seek treatment. Among those who do, many receive inadequate or nonempirically based care. Early diagnosis and appropriate treatment is clearly cost-effective, especially when compared with the cost of inadequate or ineffective treatment occurring before a correct diagnosis.[46]

Future Research Needs

Given the scope and magnitude of PTSD-related problems, private sector organizations such as the American Red Cross, federal agencies such as the Departments of Defense, Veterans Affairs, Homeland Security, DHHS, and other major stakeholders that deal with disasters and populations at increased risk for exposure to trauma need to advocate for research funding aimed at developing effective, evidence-based interventions to prevent PTSD. One key research gap is the limited ability to identify people who are at high risk of developing PTSD; this problem clearly influences what healthcare providers might (or might not) do. Thus, development of a robust clinical prediction rule that can be used to identify which recent trauma victims are at high risk of developing PTSD is an urgent need.

Conducting research immediately after a traumatic event poses inherent challenges. Future studies of PTSD prevention should adopt procedures to address these challenges and minimize problems in methods. These include improving randomization procedures; devising ways to maintain contact with patients and minimize attrition in long-term followup (e.g., tracking natural-disaster victims displaced from their homes); and bolstering analytic techniques (e.g., handling missing data, adjusting for between-group differences at baseline in all analyses).[47]

Substantial gaps exist in the current understanding of the impact of timing and dose of intervention, effectiveness in subgroups, and intervention-related harms. These factors need to be addressed first by efficacy trials. They are also relevant for comparative effectiveness trials that start treatment at different time intervals following trauma exposure or that measure time between trauma exposure and intervention and conduct preplanned subgroup analyses. Such analyses should target subgroups defined by demographic variables (e.g., gender, ethnicity); trauma type; trauma severity; and severity of baseline distress. Finally, future studies of both psychological and pharmacologic treatments should identify potential adverse effects before starting the intervention and use or adapt validated instruments to measure adverse effects.

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Appendix

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amepre.2013.02.013.